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Patient-reported adverse events and management of antifibrotic therapy in IPF: A multicenter, cross-sectional real-world study

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Abstract

Background: Antifibrotic agents slow disease progression and improve survival in IPF, yet real-life data on their use in Turkey are limited. **Objectives:** This study aimed to compare the side effects of antifibrotics in IPF patients. **Design:** A cross-sectional survey was conducted in 8 centers across 6 provinces in the Aegean Region. **Methods:** There were 470 IPF patients who completed a 30-item face-to-face questionnaire. Adverse events and their management were compared between pirfenidone and nintedanib users. **Results:** Among 470 patients, 50.6% used pirfenidone and 49.4% nintedanib. Overall, 70.6% reported at least one side effect (75.5% nintedanib vs. 66% pirfenidone, p=0.023). Medical treatment was required in 30.9% and dose reduction in 18.9%. The most common side effects were diarrhea (30.6%), appetite loss (24.9%), and nausea (22.3%). Diarrhea (p<0.001) and weight loss (p=0.010) were more frequent with nintedanib, while rash, photosensitivity, and fatigue were more common with pirfenidone (all p<0.001). Nausea, vomiting, appetite loss, and fatigue were more frequently reported in women, and vomiting, anorexia, and rash were more frequently observed in patients with comorbidities. **Conclusion:** Adverse events are frequent in IPF patients receiving antifibrotics. Nintedanib mainly causes gastrointestinal symptoms, whereas pirfenidone leads to skin reactions and fatigue. Female sex and the presence of comorbidities were associated with a higher frequency of certain adverse events. Supportive treatment and dose adjustments are crucial for maintaining adherence.

Plain language summary

This real-life study looked at side effects of the two main antifibrotic drugs (pirfenidone and nintedanib) used in idiopathic pulmonary fibrosis (IPF) in Turkey. About 7 out of 10 patients had at least one side effect. Side effects were slightly more common with nintedanib than pirfenidone. The most common side effects overall were diarrhea, loss of appetite, and nausea. Nintedanib mainly caused gastrointestinal problems, especially diarrhea and weight loss. Pirfenidone more often caused skin problems (rash, sun sensitivity) and fatigue. Women and patients with other diseases had more side effects. About 1 in 3 patients needed medication for side effects, and about 1 in 5 needed dose reduction. Side effects are common but

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manageable. The two drugs have different side effect profiles, and dose adjustment and supportive care help patients continue treatment.

Keywords
antifibrotic therapy, IPF, adverse events, nintedanib, pirfenidone, side effects

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Introduction

Idiopathic pulmonary fibrosis (IPF) is a chronic fibrosing interstitial pneumonia, which leads to respiratory failure and death within 3–5 years of diagnosis.[1] It occurs mostly in elderly patients and characterized with progressive worsening of dyspnea and decline in lung functions. Antifibrotic agents such as pirfenidone and nintedanib are recommended as first-line treatment for IPF due to their promise in slowing progression, preserving lung function and improving survival.[2]

Pirfenidone has several antiinflammatory and antifibrotic effects on fibrogenic growth factors, particularly transforming growth factor (TGF)-β1.[3] As a small molecule tyrosine kinase inhibitor, nintedanib targets the receptors of fibrosis-related kinases, including platelet-derived growth factor (PDGF), fibroblast growth factor (FGF), and vascular endothelial growth factor (VEGF).[4]

However, despite their therapeutic benefits, antifibrotic drugs can cause some adverse events. Antifibrotic therapies are mostly associated with gastrointestinal side effects.[5] Common side effects of both drugs include nausea, diarrhoea, weight loss and loss of appetite.[6] These side effects are regularly reported by patients, but there is insufficient data about their real prevalence in Turkey.

We aimed to investigate the adverse events and tolerability of two antifibrotic drugs and side effect management in patients with IPF in the Aegean Region of Turkey.

Material-method

Study design

This study was a multicentre, cross-sectional study from 8 centers in 6 provinces in the Aegean Region included 470 IPF patients treated with pirfenidone or nintedanib, which was performed in 2024.

The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement. The completed STROBE checklist has been provided as a supplementary file.[7]

The study population consisted of patients who were followed up in the ILD clinics of each study center with a diagnosis of IPF according to the European Respiratory Society/American Thoracic Society guidelines.[1] All IPF patients had been diagnosed with IPF having usual interstitial pneumonia (UIP) pattern or probable UIP pattern with the confirmation of a multidisciplinary team in each study center.

Inclusion criteria were as follows:

- adult patients (over 18 years old) with diagnosis of IPF,
- taking antifibrotic treatment (pirfenidone or nintendanib for at least three months),
- agreed to participate the study by signing the informed consent form.

Having a diagnosis of interstitial lung diseases other than IPF, having an IPF exacerbation at the time of visit, refusal to participate in the study or to join the survey were accepted as exclusion criteria.

Treatment and drug side effect information of the participants were recorded with a 30-question survey (Appendix 1), which was conducted face-to-face in the mentioned centers in 2024. This questionnaire includes questions about demographics, basic information about the use of antifibrotic drugs and adverse events that have been experienced regarding the use of pirfenidone or nintedanib. IPF treatment data including duration of treatment, adverse events of antifibrotic treatments and side effect management were also asked in the survey. Demographics and clinical data including comorbidities and medication other than IPF were checked from medical records.

Adverse events were categorized based on management approach rather than intrinsic clinical severity. Events not requiring treatment modification were classified as "manageable," while those requiring drug switch or not resolving with symptomatic treatment were classified as "events requiring treatment modification.

Treatment discontinuation was defined as the permanent withdrawal of the patients who did not receive their planned antifibrotics due to side effects or clinical unresponsiveness. There may be the switch of antifibrotics (pirfenidone to nintedanib or nintedanib to pirfenidone), permanent withdrawal or dose reduction. In "switch" group, adverse events were attributed to the specific antifibrotic drug that led to treatment modification or switching, rather than the current treatment at the time of the survey. Therefore, adverse events were recorded in relation to the drug considered responsible for the event, based on patient report and hospital data.

Sample size calculation was performed using G*Power 3.1 software based on data from a previously published similar study.[5] Assuming a power of 80%, a type I error rate of 5%, the required sample size was calculated as 305 patients. Considering a potential 10% loss to follow-up or incomplete data, the target sample size was increased to 336 accordingly.

Freely-given, written informed consent to participate in the study was obtained from all individual participants prior to their inclusion. The informed consent statement has been revised throughout the manuscript to ensure consistency and clarity. We confirm that written informed consent was obtained from all participants (or from their legal guardians where applicable) prior to inclusion in the study, in accordance with institutional ethical standards and the Declaration of Helsinki.

Statistical analysis

The statistical analyses were performed by using the Statistical Package for the Social Sciences (SPSS) version 27.0 (IBM Corp., Armonk, NY). Chi-square or Fisher's Exact tests were used for the analysis of categorical variables. Descriptive statistics included mean and standard deviation for continuous variables, and numbers and percentages for categorical variables. Kolmogorov-Smirnov and Shapiro-Wilk tests were employed to assess the normality of continuous variables across the groups, while parametric tests (Independent samples t-test) were used for independent variables that followed a normal distribution and non-parametric tests (Mann-Whitney U test) for variables that did not adhere to a normal distribution. Correlations between continuous variables were evaluated using correlation coefficients with parametric tests (Pearson's) or non-parametric tests (Spearman's), depending on the normality of the distribution. The statistical significance level was set at 0.05.

Results

Of the 470 patients included in the study, 364 were male (77.4%) and the mean age was 68.8±7.5. There were 238 IPF patients (50.6%) who were using pirfenidone and 232 (49.4%) using nintedanib. Demographics and some features due to antifibrotics are in table 1.

There was at least one comorbidity other than IPF in 65.3% of patients (307/470). There was no significant difference between pirfenidone and nintedanib patients among the presence of comorbidities (p=0.117). Hypertension (20.9%), gastroesophageal reflux disease (16.6%) and diabetes mellitus (8.8%) were the most common comorbidities. The number of comorbidities per patient was found to be 1.07 ± 0.16.

Table 1. Demographics and features of IPF patients according to using antifibrotics.

Features	Total population (n = 470)	Patients using nintedanib (n=232)	Patients using pirfenidone (n=238)	P value
Gender (male/female, %)	364/106,79.1/20.9%	178/54, 76.7/23.3%	186/52, 78.2/21.8%	0.711
Age (mean)	68.8 ± 7.5	68.4±7.4	69.3±7.6	0.197
Comorbidities (present/not, %)	307/163, 65.3/34.7%	14/88, 62.1/37.9%	163/75, 68.5/31.5%	0.144
Number of comorbidities (/per patient)	1.07 ± 0.16	1.03 ± 0.09	1.10 ± 0.11	0.451
Active smoking (yes/no)	53/417, 11.3/88.7%	28/204, 12.1/87.9%	25/213, 10.5/89.5%	0.211
Package.year (mean)	34.3±5.2	26.4±2.7	26.9±2.8	0.592
FEV1 (%, mean)	79.2±18.0	78.8±17.9	79.2±19.0	0.840
FVC (%, mean)	75.4±17.4	74.9±16.3	76.0±18.4	0.460
DLCO (%, mean)	54.6±18.7	54.1±19.5	55.2±17.9	0.530
Number of AE (/per patient)	1.77 ± 0.89	1.93 ± 0.97	1.60 ± 0.81	0.060

FEV1: Forced expiratory volume in 1 second; FVC: Forced vital capacity; DLCO: Diffusing capacity of the lung, IPF: Idiopathic pulmonary fibrosis.

At least one side effect was detected during the IPF treatment process in 70.6% (332/470) of the patients (75.5% in nintedanib, 66% in pirfenidone, p=0.023). Demographics and some features between groups with and without adverse events are in table 2.

The most common side effects were recorded as diarrhea (30.6%), loss of appetite (24.9%) and nausea (22.3%). Most adverse events (87.6%) were manageable without treatment modification, while 12.4% required treatment modification.

Diarrhea (p<0.001) and weight loss (p=0.010) were found to be significantly higher in patients using nintedanib, while rash (p<0.001), photosensitivity (p<0.001) and fatigue (p<0.001) were found to be significantly higher in patients using pirfenidone compared to the other treatment group (table 3).

Most of the side effects were managed with supporting therapies and dose reductions: 30.9% used medical treatment due to side effects, and 18.9% had their IPF medication dose reduced.

While nausea, vomiting, fatigue and loss of appetite were statistically more common in women (p=0.023, 0.043, 0.001 and p<0.001, respectively), vomiting (p=0.006), anorexia (p=0.016) and rash (p=0.041) were more frequently reported in those with comorbidities.

Use of additional medications due to side effects was observed to be in the presence of diarrhea (p<0.001), nausea (p=0.037) and vomiting (p=0.001), and the reduction of antifibrotic drug dose was found to be significantly higher in diarrhea (p=0.015) and increased liver enzymes (p=0.004).

Switching first-line antifibrotic drug was in 10.9% (from pirfenidone to nintedanib:66.7%, nintedanib to pirfenidone: 33.3%, p=0.020) of IPF patients. It was required due to intolerable adverse effects in 83.7% or disease progression in 16.3%. The most common reason for switch was rash (61.3%, p<0.001) and photosensitivity in pirfenidone (48.4%, p<0.001), and stomachache (47.1%, p=0.001) and diarrhea (41.2%, p=0.395) in nintedanib group. Treatment discontinuation happened in 1.9% of patients. There was no significant difference between two antifibrotic drugs among discontinuation (p=0.468).

However, because permanent treatment discontinuation occurred in only 1.9% of patients, a formal multivariable analysis for discontinuation risk factors was not statistically feasible.

Discussion

This study represents one of the largest real-world analyses examining the safety and tolerability of antifibrotic drugs among IPF patients in Turkey. Our findings suggest that diarrhea and weight loss are significantly more common in patients treated with nintedanib, while rash, photosensitivity, and fatigue are more prevalent among pirfenidone users. Our results revealed that female gender and the presence of comorbidities are conditions that require more attention regarding drug tolerance. Temporary dose reduction or additional medical treatment in side effect management is important to ensure continuity of antifibrotic treatment. These results align with existing literature and emphasize the need for careful monitoring of side effects.

Antifibrotic therapies such as pirfenidone and nintedanib are the cornerstone treatments for IPF and have demonstrated efficacy in slowing disease progression and preserving lung function.[8] However, there were side effects detected due to antifibrotics in more than two thirds of our patients, which is similar to other studies. *Ortiz* et al. described 64.1% of their study population having adverse effects.[9] We can say that side effects are relatively common with antifibrotics. Considering that adverse events have a high incidence, this monitoring should be done more carefully and intensively.

Table 2. Demographics and features of IPF patients with or without adverse events.

Features	Total population (n = 470)	Patients with AE (n=332)	Patients without AE (n=138)	P value
Gender (male/female, %)	364/106, 79.1/20.9%	178/54, 76.7/23.3%	186/52, 78.2/21.8%	0.711
Age (mean)	68.8 ± 7.5	69.1 ± 7.2	68.1±8.1	0.152
Comorbidities (present/not, %)	222/110, 66.9/33.1%	85/53, 61.6/38.4%	163/75, 68.5/31.5%	0.309
Number of comorbidities (/per patient)	1.07 ± 0.16	1.10 ± 0.17	0.99 ± 0.11	0.335
Active smoking (yes/no)	53/417, 11.3/88.7%	33/299, 11/89%	20/118, 16.9/83.1%	0.078
Package.year (mean)	34.3±5.2	35.2±5.8	32.1±4.8	0.116
FEV1 (%, mean)	79.2±18.0	79.7±18.4	78.0±17.3	0.473
FVC (%, mean)	75.4±17.4	76.1±17.4	73.8±17.8	0.126
DLCO (%, mean)	54.6±18.7	55.1±18.9	53.5±18.1	0.286

AE: Adverse events, FEV1: Forced expiratory volume in 1 second; FVC: Forced vital capacity; DLCO: Diffusing capacity of the lung, IPF: Idiopathic pulmonary fibrosis.

Table 3. Adverse events during antifibrotic treatment.

Side effects	IPF patients using nintedanib (n=232)	IPF patients using pirfenidone (n=238)	P value
Diarrhoea (yes/no, %)	121/111, 52.1%	24/214, 10.1%	**<0.001**
Nausea (yes/no, %)	54/178, 23.3%	52/186, 21.8%	0.711
Vomiting (yes/no)	24/208, 10.3%	17/221, 7.1%	0.219
Weight loss (yes/no)	64/168, 27.6%	38/200, 19%	**0.010**
Rash (yes/no)	17/215, 7.9%	52/186, 28%	**<0.001**
Photosensitivity (yes/no)	0/231, 0%	30/211, 14.2%	**<0.001**
Fatigue (yes/no)	28/204, 13.7%	67/171, 39.2%	**<0.001**
Bleeding (yes/no)	6/226, 2.7%	4/234, 1.7%	0.496
Anorexia (yes/no)	58/174, 33.3%	59/179, 33%	0.958
Liver function test abnormality (yes/no)	8/224, 3.6%	7/231, 3%	0.755
Stomachache (yes/no)	38/194, 19.6%	33/205, 16.1%	0.447
Headache (yes/no)	16/216, 7.4%	21/217, 9.7%	0.438

IPF: Idiopathic pulmonary fibrosis.

Gastrointestinal side effects, particularly diarrhea, were the most commonly reported adverse events, especially among patients using nintedanib. Our findings are consistent with previous trials, as well as real-world studies showing nintedanib's association with gastrointestinal symptoms. In the VigiAccess database, gastrointestinal disorders, including nausea, vomiting and diarrhoea account for majority adverse events of reports.[10]

The current study showed that nintedanib causes a significant increase in adverse events, especially in diarrhea and weight loss. *Komatsu* et al.[11] demonstrated that IPF patients experienced more adverse events from nintedanib, especially in elder population.[10] *Proesmans* et al. revealed that diarrhoea, vomiting, weight loss and loss of appetite were significantly higher in patients using nintedanib.[6] Diarrhea and nausea were reported as the most frequent side effects among IPF patients using nintedanib in INPULSIS-1.[12] In the INPULSIS trials, diarrhea was reported in approximately 62% of patients receiving nintedanib, which is comparable to our real-world findings showing diarrhea in 52.1% of patients. These results exhibit that nintedanib is associated with a higher rate of gastrointestinal adverse effects when compared with pirfenidone.

On the other hand, pirfenidone was more often associated with dermatological reactions like rash and photosensitivity, and systemic symptoms such as fatigue. These effects have been previously reported and are well-documented in patients treated with pirfenidone. Although nausea and fatigue are more common adverse events, some patients being treated with pirfenidone experienced skin rashes and photosensitivity.[13] Pirfenidone-related rash and photosensitivity observed in our cohort are also consistent with previous randomized controlled trials such as ASCEND and CAPACITY, where photosensitivity and skin-related adverse events were among the most frequently reported treatment-related side effects.[14,15] Patients taking pirfenidone may have skin-related adverse effects, but those on nintedanib predominantly had gastrointestinal problems.

Notably, women were found to experience adverse effects such as nausea, vomiting, anorexia and fatigue more frequently, consistent with previous findings suggesting gender-based differences in drug tolerability. *Ortiz* et al. revealed that women were more likely to have adverse events and withdraw from antifibrotic treatment due to side effects.[9] Therefore, management of antifibrotic-related side effects should be given special attention in women.

Similarly, IPF patients with comorbidities showed higher rates of vomiting and rash. Most patients suffering from IPF are older and have more comorbidities, which may lead to more medication use, interactions, and consequently more side effects.[16,17] As a result, comorbidities can affect drug tolerability in patients with fibrotic interstitial lung disease.

Supportive therapies and temporary dose reductions were effective in managing most side effects such as diarrhea, nausea and vomiting. In most studies, the gastrointestinal adverse events can be managed through measures to manage symptoms with added drugs such as loperamide or metpamide.[18] As continuation of antifibrotics is an important issue, supporting care including antidiarrheal or antiemetic therapy should be evaluated for patients with high risk potential of gastrointestinal disorders.

Dose reductions due to diarrhea and elevated liver enzymes were also significant according to our results. Diarrhea caused by nintedanib may be suppressed not only by the use of antidiarrheal medication, but also by dose reduction as well.[19] Patients who develop aminotransferase elevations on therapy should also be monitored more carefully and considered for dose reduction with close follow up. Temporary or permanent dose reduction is advised for management of adverse reactions or poor tolerability. In clinical practice, adjusting dosage may help patients remain on treatment longer, thereby improving long-term outcomes.

Regarding drug tolerability, our results are similar with previous reports.[5,20] Despite the high prevalence of side effects (especially diarrhea and weight loss with nintedanib, and rash and fatigue with pirfenidone), most of them were managed with supportive treatment and temporary dose reductions. Discontinuation of the therapy was only in a small group, which may suggest acceptable tolerability in patients who were able to continue treatment; however, this finding should be interpreted with caution due to potential selection bias.

Although not routinely practiced, switching drugs can be an effective strategy for patients who are unable to tolerate a specific agent or show disease progression under treatment. Switching antifibrotic agents due to side effects or disease progression was necessary in a small but notable portion of the cohort. *Çilli* et al. revealed there was switch in 10.5% of their IPF patients who had received antifibrotics eventually switched drugs, while the most common reason for the switch was found as disease progression.[21] Our switch rate (10.9%), with the most common reason being intolerable side effects, aligns with other real-world reports, which range from 4% to 53%.[22]

The permanent discontinuation rate in our cohort was relatively low (1.9%) compared with rates reported in randomized controlled trials and real-world studies, where discontinuation rates generally range between 10% and 30%.[20–22] This difference may partly be explained by the cross-sectional design of our study and the inclusion criterion requiring at least three months of treatment exposure, which may have excluded patients with early intolerance. Additionally, as permanent treatment discontinuation occurred in only 1.9% of patients, a formal multivariable analysis for discontinuation risk factors was not statistically feasible.

Our study has some limitations. The main limitation of this study is its cross-sectional and retrospective design based on patient-reported adverse events. While this approach reflects real-world patient experience, it limits the ability to directly compare tolerability between treatments or to attribute adverse events causally to a specific drug. Also, due to the observational design, risk factor analyses for the development of adverse events and discontinuation of antifibrotic treatment could not be comprehensively performed. Recall bias is likely, particularly given the elderly IPF population, and some symptoms such as fatigue, anorexia, and weight loss may be related to the underlying disease rather than treatment itself. Also, the questionnaire was pilot-tested and not formally validated, which is also another limitation. A prospective, longitudinal follow-up would provide more robust and objective data.

In addition, only patients who had received antifibrotic therapy for at least three months were included. This may have excluded patients who discontinued treatment early. Poor tolerability, introducing a potential survivor bias and leading to an underestimation of clinically relevant intolerance. Detailed treatment-related variables such as exact treatment duration, time to onset of adverse events, and prior dose reductions were not consistently available or analyzed, which limits a more comprehensive evaluation of treatment tolerability. Although certain adverse events appeared more frequently in women and in patients with comorbidities, no significant association was observed between overall adverse event occurrence and these variables. Therefore, multivariable logistic regression analysis for overall adverse events was not considered appropriate.

Conclusion

Adverse effects related to antifibrotic treatments are commonly observed in IPF patients. Diarrhea and weight loss are more frequently associated with nintedanib, while rash (including photosensitivity) and fatigue are more common with pirfenidone. Female sex and the presence of comorbidities were associated with higher reporting of adverse events. Managing side effects with supportive treatments and dose adjustments is essential to maintain continuity in antifibrotic therapy.

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Ethical considerations

The study protocol was approved by the Ethics Committee of Izmir Katip Celebi University in accordance with the principles of the Declaration of Helsinki (Date: 21.03.2024; approval number: #0113).

Consent to participate

Freely-given, written informed consent to participate in the study was obtained from all individual participants prior to their inclusion.

Consent for publication

The manuscript does not contain any individual patient data, images, or videos requiring specific publication consent.

Author contributions

Methodology, Software, Validation, Formal Analysis, Writing – Original Draft: Onur Turan. Investigation, Data Curation, Resources, Writing – Review & Editing, Project Administration, Funding Acquisition, Visualization, Supervision: Onur Turan, Erhan Uğurlu, Özge Oral Tapan, Nurhan Sarıoğlu, Gülru Polat, Şule Çilekar, Özgür Batum, Şule Taş Gülen.

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Data Availability Statement

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Appendix

Appendix 1 – IPF PATIENT QUESTIONNAIRE

1. Your name and surname:
2. Gender: A. Male B. Female
3. Your marital status:

A. Married B. Single C. Divorced

4. Your age: A. Under 40 B. 40-50 C. 51-60 D. Over 60 5. The city you live in: A. İzmir B. Aydın C. Manisa D. Denizli E. Afyon F. Balıkesir G. Muğla H. Other (……)
6. Do you have any other diseases other than lung hardening? A. No B. Yes (……..)
7. Do you smoke? A. Yes B. Never smoked C. Quit
8. What medication have you used for lung hardening?
   a) Pirfenidone
   b) Nintedanib
   c) I used both medications
9. Which medication are you using now?
   a) Pirfenidone b) Nintedanib c) None
10. Are you taking any medications for this or another illness? a) No b) Yes Please specify…….

Patients who are using/have used pirfenidone will answer the following questions.

How many mg of the medication do you use?
a)200 b) 267 c) 600 d) 801
Frequency of use:
a) 4 times a day b) 3 times a day c) 2 times a day d) 1 time a day How many do you take each time you use it? a) 1 b) 2 c) 3 d) 4

Which of the following side effects did you experience/do you experience while using the medication?

1) diarrhea, a) Yes b) No
2) nausea, a) Yes b) No
3) headache a) Yes b) No
4) skin reactions and rash (after exposure to sunlight) a) Yes b) No
5) weakness, a) Yes b) No
6) decreased appetite a) Yes b) No
7) abdominal pain a) Yes b) No
8) vomiting a) Yes b) No
9) weight loss a) Yes b) No
10) Other: specify……

Patients who use/have used nintedanib will answer the following questions.
How much mg of nintedanib are you using? a)150 b) 100

Frequency of use: a) Twice a day d) Once a day

Which of the following side effects did you experience/do you experience while using the drug?

1) diarrhea, a) Yes b) No
2) nausea, a) Yes b) No
3) vomiting, a) Yes b) No
4) rash, a) Yes b) No
5) bleeding, a) Yes b) No
6) weight loss, a) Yes b) No
7) decreased appetite a) Yes b) No
8) abdominal pain a) Yes b) No
9) headache a) Yes b) No
10) increased blood pressure a) Yes b) No
11) increased liver enzymes (as stated by your doctor)
12) Other: specify……

The following questions will be answered regarding the observed side effects.
Frequency of occurrence of the current side effect: a) daily b) once a week or a few days c) once a month or a few days
Has a medication been prescribed to relieve this problem due to the side effect? a) no b) yes (if yes…….)
Has the dosage of the medication you are using been changed due to the side effect? a) no b) yes.
Has the medication you are using been changed due to the side effect? a) no b) yes.
Have you stopped this medication/has your doctor stopped it permanently because of side effects? a) no b) yes.